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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,352	01/21/2000	JAAP GOUDSMIT	T/97300 US	6213

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EXAMINER
SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
1634	20

DATE MAILED: 04/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/463,352	GOUDSMIT ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Group 1630, Art Unit 1634, and has been assigned to Primary Examiner Bradley L. Sisson.

Continued Prosecution Application

2. The request filed on 31 January 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/463,352 is acceptable and a CPA has been established. An action on the CPA follows.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-9, 11, and 12 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As presently worded, claims 1-4 are drawn to oligonucleotides that can be from 10 to 50 nucleotides in length; and claims 8 and 9 are drawn to kits that comprise said sequences while claims 5-7 and 11-12 are drawn to methods whereby said

oligonucleotides are used to detect a viral target. Upon review of the disclosure it is noted that the specification does not provide an adequate written description of the entire sequences of these oligonucleotides, especially as it relates to sequences greater in size to the disclosed sequences and/or comprise nucleotides other than what are described in the disclosure. The specification, rather than defining the sequences in terms of their structure is attempting to define the oligonucleotides in terms of how they are to function and seek to encompass all that would work. Such an attempt to claim not in terms of structure but in terms of function does not constitute an adequate written description of the sequences, nor does it demonstrate possession of the genus of sequences now claimed. *Enzo v. Gen-Probe* (CAFC 01-1230, April 2, 2002).

5. Claims 1-9, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth above, the claims encompass oligonucleotide sequences tht are not adequately described by the disclosure and to which the specification does not reasonably suggest that applicant was in possession of the complete genus of sequences encompassed by the claims. It is well settled that one cannot enable the use of a compound or product that they do not possess nor which is adequately described. *University of California v. Eli Lilly and Co.* (CA FC, July 1997) 43 USPQ2d 1398.

Claim Rejections - 35 USC § 102/103

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1-5, 7-9 and 11-12 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Backus et al.

8. Backus et al., disclose oligonucleotide primers that are to be used in a method whereby HIV-1 can be detected. As seen in column 11, oligonucleotides corresponding to SEQ ID NO:2, 4, and 24 comprise the nucleotide sequence as found in applicants oligonucleotides represented by SEQ ID NO:1, 2, 4, 5.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-9, 11, and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Montagnier et al., in view of Backus et al., and Research Genetics.

13. Montagnier et al., column 19, third paragraph, bridging to column 20, disclose primers for detecting HIV-1 and methods of doing same. At column 19, last paragraph, bridging to column 20, first two lines, Montagnier et al., teach explicitly of directing primers to conserved regions and specifically teaches that one such region of conserved sequences is found in the long terminal repeat, or LTR. It is noted that the LTR is the very region from which applicant has selected the instantly claimed primers/probes; see the response of 26 December 2000, page 7, lines 13-15, wherein is stated:

> The primers of the present invention are not from the GAG region, but instead are from the long terminal repeat (LTR) of HIV-1."

It is abundantly clear that Montagnier et al., are directing the public to this very region for the selection of primers and probes. Furthermore, they provide motivation in selecting sequences that allow for the detection of multiple isolates when they teach that the LTR is "highly conserved."

14. Montagnier et al., column 20, second paragraph, teach that RT-PCR can be practiced and that such allows for the detection of viral sequences in individuals before they seroconvert.

15. Backus et al., disclose oligonucleotide primers that are to be used in a method whereby HIV-1 can be detected. As seen in column 11, oligonucleotides corresponding to SEQ ID NO:2, 4, and 24 comprise the nucleotide sequence as found in applicants oligonucleotides represented by SEQ ID NO:1, 2, 4, 5.

16. Research Genetics, through their advertisement, disclose for sale software that allows the ordinary artisan to set parameters whereby the software will automatically screen all possible sequence comparisons and provide a listing of those primers that meet the established criteria. As seen in the publication, such parameters to be employed in the selection of primer and probe sequences include desired specificity, length, GC content, secondary structure characteristics, etc.

17. It would have been obvious to one of ordinary skill in the art at the time the instantly claimed invention was made to have used the software of Research Genetics with the teachings of Backus et al., and Montagnier et al., so to select primers and probes form the LTR region of HIV-1 where such sequences are identified through the use of the commercially available

sequence screening software. With Montagnier et al., teaching explicitly how to identify and make primers that in turn comprise highly conserved HIV-1 LTR sequences as well as the use of such primers in PCR reactions, and with Backus teaching these very sequences, and with the straightforward, Windows-based software allowing for the ready identification of just such conserved sequences between isolates, the skilled artisan would have reasonably expected to have identified primers of an appropriate length and which are comprised of the now claimed conserved nucleotide sequence. Said artisan would have been motivated to have used primers that anneal to highly conserved HIV-1 LTR regions as Montagnier et al., explicitly teaches performing PCR on HIV-1 as well as the production of primers directed to highly conserved HIV-1 LTR regions.

18. Applicant's statements to their ability to detect all known isolates of HIV-1 through the use of their primers/probes, in light of the explicit teachings of Montagnier et al., do not rise to the level of a an unexpected and non-obvious quality. Additionally, the claims, as presently written, do not support the assertion of any unexpected result. It is noted with particularity that the primers are to be (a) derived from SEQ ID NO:1-5 and 12, and that they can be from 10-50 nucleotides in length. None of the sequences represented by SEQ ID NO:1-5 or 12 are 50 nucleotides in length. As seen below in the following chart, the sequences set forth in the claims, e.g., claim 1, are all far short of the claimed upper length allowed for the primers.

SEQ ID NO.	Length	No. of Additional Nucleotides that can be Added
1	18	32
2	20	30
3	15	35
4	20	30
5	20	30

12	30	20

It is noted with particularity that with the primers being any where from 10 to 50 nucleotides in length, any with there being a minimum of 10 nucleotides being used from each of SEQ ID NO:1-5 and 12, the claims encompass a nearly limitless number of probes . Support for this position is based in part on the claims encompassing primers of 50 nucleotides in length yet only 10 of the nucleotides being from any one of the sequences represented by a SEQ ID NO., e.g., SEQ ID NO:1. Accordingly, and using for example a probe of 50 nucleotides in length, and with there being 9 possible 10mers derived from SEQ ID NO:1, there are 9×4^{40} or 1.08×10^{28} possible probes. The number of probes is compounded even further when one contemplates the number of possible probes when the number of nucleotides added can range from 1 to 39, and then to recompute for 11mers, 12mers, etc., being derived from just SEQ ID NO:1, and then start anew for SEQ ID NOs: 2, 3, 4, 5, and 12. Clearly, the evidence of record is insufficient to support that such an immense genus of sequences, as a whole, exhibit an unusual or unexpected property.

19. To further cast doubt on the inability of the majority of the members of the genus to exhibit an unexpected property, attention is directed to the publication of Sommer and Tautz which show that effective priming was achieved with as little as three nucleotides matching at the 3' end of the primer. In light that there is no requirement that the additional 1 to 40 nucleotides added to the essential 10mer not be from HIV-1, much less a conserved region of an LTR of HIV-1, the likelihood of irrelevant sequences imparting the asserted unexpected property is most unlikely.

20. Accordingly, the rejection under 35 USC 103(a) has not been found to be lessened by a secondary consideration.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

bls
April 3, 2002